

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently Amended) A method for predicting the risk of the occurrence of granulocytopenia caused by paclitaxel therapy in a subject comprising identifying in a gene isolated from the subject one or more genetic polymorphisms selected from ~~the group consisting of:~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 2 in CYP2C8 gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 3 in CYP2C8 gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 5 in CYP2C8 gene,~~

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene,

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 7 in BUB1b gene,

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 8 in BUB1b gene,



a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 9 in BUB1b gene, and

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 10 in BUB1b gene, and

assessing a genotype(s) of said one or more genetic polymorphisms to thereby predict the risk of the occurrence of granulocytopenia caused by paclitaxel therapy in said subject.

2. (Withdrawn) The method according to claim 1, wherein the risk of the occurrence of granulocytopenia is predicted to be high in the case where the gene isolated from the subject is one or more of the following (a) through (e):

(a) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene is G/G;

(b) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 2 in CYP2C8 gene is T/T;

(c) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 3 in CYP2C8 gene is G/G;

(d) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene is T/T; and

(e) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 5 in CYP2C8 gene is G/G.



3. (Withdrawn) The method according to claim 1, wherein the risk of the occurrence of granulocytopenia is predicted to be low in the case where the gene isolated from the subject is one or more of the following (f) through (j):

(f) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene is A/G or A/A;

(g) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 2 in CYP2C8 gene is C/T or C/C;

(h) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 3 in CYP2C8 gene is A/G or A/A;

(i) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene is A/T or A/A; and

(j) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 5 in CYP2C8 gene is A/G or A/A.

4. (Currently Amended) The method according to claim 1, wherein the risk of the occurrence of granulocytopenia is predicted to be high in the case where the gene isolated from the subject exhibits one or more of the following (A) through (E):

(A) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene is A/A;

(B) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 7 in BUB1b gene is T/T;

(C) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 8 in BUB1b gene is C/C;



(D) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 9 in BUB1b gene is C/C; and

(E) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 10 in BUB1b gene is T/T.

5. (Currently amended) The method according to claim 1, wherein the risk of the occurrence of granulocytopenia is predicted to be low in the case where the gene isolated from the subject ~~[[is]]~~ exhibits one or more of the following (F) through (J):

(F) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene is A/G or G/G;

(G) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 7 in BUB1b gene is G/T or G/G;

(H) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 8 in BUB1b gene is C/T or T/T;

(I) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 9 in BUB1b gene is C/T or T/T; and

(J) the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 10 in BUB1b gene is C/T or C/C.

6. (Withdrawn-Currently amended) The method of claim 1, A method for predicting  
~~the risk of the occurrence of granulocytopenia caused by paclitaxel therapy in a subject~~  
further comprising:

~~(1) a step of~~ identifying in a gene isolated from the subject one or more genetic polymorphisms selected from the group consisting of:



a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

1 in CYP2C8 gene,

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

2 in CYP2C8 gene,

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

3 in CYP2C8 gene,

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

4 in CYP2C8 gene, and

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

5 in CYP2C8 gene; and

~~(2) a step of identifying in a gene isolated from the subject one or more genetic polymorphisms selected from the group consisting of:~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:~~

~~6 in BUB1b gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:~~

~~7 in BUB1b gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:~~

~~8 in BUB1b gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:~~

~~9 in BUB1b gene, and~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:~~

~~10 in BUB1b gene.~~



7. (Withdrawn) The method according to claim 6 comprising identifying in a gene isolated from the subject a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene, and a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene.

8. (Withdrawn) The method according to claim 7, wherein the risk of the occurrence of granulocytopenia is predicted to be high when the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene is T/T, and the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene is A/A or G/G.

9. (Withdrawn) The method according to claim 7, wherein the risk of the occurrence of granulocytopenia is predicted to be low when the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene is A/T or A/A, and the genotype at the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene is A/G.

10. (Withdrawn - Currently amended) A diagnostic kit for predicting the risk of the occurrence of granulocytopenia caused by paclitaxel therapy in a subject comprising a reagent for identifying in a gene isolated from the subject one or more genetic polymorphisms selected from the group consisting of:  
~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene,~~



~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:~~

~~2 in CYP2C8 gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:~~

~~3 in CYP2C8 gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:~~

~~4 in CYP2C8 gene,~~

~~a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:~~

~~5 in CYP2C8 gene,~~

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

6 in BUB1b gene,

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

7 in BUB1b gene,

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

8 in BUB1b gene,

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

9 in BUB1b gene, and

a genetic polymorphism at the 11th nucleotide of the sequence defined by SEQ ID NO:

10 in BUB1b gene.

11. (Withdrawn - Currently amended) The diagnostic kit according to claim 10,

wherein the reagent comprises one or more nucleic acid molecules selected from

~~the group consisting of:~~

a nucleic acid molecule having:



~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene, or a sequence complementary thereto; or~~

~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene, or a sequence complementary thereto;~~

a nucleic acid molecule having:

~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 2 in CYP2C8 gene, or a sequence complementary thereto; or~~

~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 2 in CYP2C8 gene, or a sequence complementary thereto;~~

a nucleic acid molecule having:

~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 3 in CYP2C8 gene, or a sequence complementary thereto; or~~

~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 3 in CYP2C8 gene, or a sequence complementary thereto;~~

a nucleic acid molecule having:

~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene, or a sequence complementary thereto; or~~



~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene, or a sequence complementary thereto;~~

~~a nucleic acid molecule having:~~

~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 5 in CYP2C8 gene, or a sequence complementary thereto; or~~

~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 5 in CYP2C8 gene, or a sequence complementary thereto;~~

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene, or a sequence complementary thereto; or

a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene, or a sequence complementary thereto;

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 7 in BUB1b gene, or a sequence complementary thereto; or

a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 7 in BUB1b gene, or a sequence complementary thereto;



a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 8 in BUB1b gene, or a sequence complementary thereto; or  
a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 8 in BUB1b gene, or a sequence complementary thereto;

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 9 in BUB1b gene, or a sequence complementary thereto; or  
a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 9 in BUB1b gene, or a sequence complementary thereto; and

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 10 in BUB1b gene, or a sequence complementary thereto; or  
a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 10 in BUB1b gene, or a sequence complementary thereto.

12. (Withdrawn - Currently amended) The diagnostic kit according to claim ~~[[10]]~~ 11, wherein the reagent further comprises:



~~(1)~~—one or more nucleic acid molecules selected from the group consisting of:

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene, or a sequence complementary thereto; or

a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene, or a sequence complementary thereto;

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 2 in CYP2C8 gene, or a sequence complementary thereto; or

a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 2 in CYP2C8 gene, or a sequence complementary thereto;

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 3 in CYP2C8 gene, or a sequence complementary thereto; or

a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 3 in CYP2C8 gene, or a sequence complementary thereto;

a nucleic acid molecule having:



a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene, or a sequence complementary thereto; or

a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene, or a sequence complementary thereto; and

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 5 in CYP2C8 gene, or a sequence complementary thereto; or

a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 5 in CYP2C8 gene, or a sequence complementary thereto; and

~~(2) one or more nucleic acid molecules selected from the group consisting of:~~

~~a nucleic acid molecule having:~~

~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene, or a sequence complementary thereto; or~~

~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene, or a sequence complementary thereto;~~

~~a nucleic acid molecule having:~~



~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 7 in BUB1b gene, or a sequence complementary thereto; or~~

~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 7 in BUB1b gene, or a sequence complementary thereto;~~

a nucleic acid molecule having:

~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 8 in BUB1b gene, or a sequence complementary thereto; or~~

~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 8 in BUB1b gene, or a sequence complementary thereto;~~

a nucleic acid molecule having:

~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 9 in BUB1b gene, or a sequence complementary thereto; or~~

~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 9 in BUB1b gene, or a sequence complementary thereto; and~~

a nucleic acid molecule having:

~~a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 10 in BUB1b gene, or a sequence complementary thereto; or~~



~~a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 10 in BUB1b gene, or a sequence complementary thereto.~~

13. (Withdrawn) The diagnostic kit according to claim 10, wherein the reagent comprises:

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene, or a sequence complementary thereto; or

a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene, or a sequence complementary thereto; and

a nucleic acid molecule having:

a sequence of at least 10 contiguous nucleotides containing the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene, or a sequence complementary thereto; or

a sequence of at least 10 contiguous nucleotides adjacent to the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene, or a sequence complementary thereto.

14. (Withdrawn - Currently amended) The diagnostic kit according to claim 10, wherein the reagent is one or more PCR primer pairs selected from the group consisting of:



~~a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene;~~

~~—— a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 2 in CYP2C8 gene;~~

~~—— a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 3 in CYP2C8 gene;~~

~~—— a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene;~~

~~—— a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 5 in CYP2C8 gene;~~

a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene;

a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 7 in BUB1b gene;

a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 8 in BUB1b gene;



a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 9 in BUB1b gene; and,

a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 10 in BUB1b gene.

15. (Withdrawn - Currently amended) The diagnostic kit according to claim ~~[[10]]~~ 14, wherein the reagent further comprises:

~~(4) — one or more PCR primer pairs selected from the group consisting of:~~

a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 1 in CYP2C8 gene;

a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 2 in CYP2C8 gene;

a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 3 in CYP2C8 gene;

a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene; and



a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 5 in CYP2C8 gene; and

~~(2) — one or more PCR primer pairs selected from the group consisting of:~~

~~a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene;~~

~~a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 7 in BUB1b gene;~~

~~a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 8 in BUB1b gene;~~

~~a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 9 in BUB1b gene; and~~

~~a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 10 in BUB1b gene.~~

16. (Withdrawn) The diagnostic kit according to claim 10, wherein the reagent comprises:



a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 4 in CYP2C8 gene; and

a PCR primer pair designed so as to amplify DNA corresponding to the region containing the 11th nucleotide of the sequence defined by SEQ ID NO: 6 in BUB1b gene.